



Published in final edited form as:

Int J Drug Policy. 2018 May ; 55: 113–120. doi:10.1016/j.drugpo.2018.02.020.

Factors associated with concurrent heroin use among patients on methadone maintenance treatment in Vietnam: A 24-month retrospective analysis of a nationally representative sample

Thai Hoang^{1,*}, Hong Nguyen¹, Ray W. Shiraishi³, Mai Nguyen², Trista Bingham³, Diep Nguyen², Tam Nguyen², Hao Duong^{1,4}, Sheryl Lyss¹, and Hien Tran²

¹Centers for Diseases Control and Prevention – Division of Global HIV and TB, Vietnam Country Office

²Vietnam Administration of HIV/AIDS Control

³Centers for Diseases Control and Prevention – Division of Global HIV and TB

⁴The Partnership for Health Advancement in Vietnam (HAIVN)

Abstract

Background—Methadone maintenance treatment (MMT) is highly effective for reducing heroin use and HIV transmission among people who inject opioids. We sought to measure and understand factors associated with continued heroin use, a critical outcome among MMT patients in Vietnam.

Method—We abstracted data from medical charts of nationally representative sample of patients who were on MMT during May 2008–December 2013, selecting 10 MMT clinics using probability proportional to size and 50 patients/clinic by systematic random sampling. Concurrent heroin use was defined by self-report/positive urine test recorded in patient charts during month 3, 6, 12, and 24 after MMT initiation. We used multivariable logistic regression to identify factors associated with concurrent heroin use over the first 24 months in treatment.

Results—All clients used heroin at baseline; concurrent heroin use was 55% at month 3; 19%, 14.6% and 15.2% at month 6, 12, and 24, respectively. Having no baseline family emotional/financial support versus having (AOR=2.03; 95% confidence interval [CI]=1.17–3.53); using heroin for <15 years versus 15 years at baseline (AOR=1.55; 95% CI=1.01–2.38); being HIV-infected/not on antiretroviral treatment (ART; AOR=1.79; 95% CI=1.07–2.98) or being HIV infected/on ART (AOR=2.39; 95% CI=1.61–3.55), versus not being HIV infected; baseline

Corresponding author: Thai Hoang; CDC – The U.S Embassy in Hanoi, no7 Lang Ha, Ba Dinh, Hanoi, Vietnam; Phone: +84 904851011; Fax: +84 24 3935 1918; vph6@cdc.gov.

DECLARATIONS

The authors declare no conflicts of interest.

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention or of the Agency for Toxic Substances and Disease Registry.

Authors' contributions: TH, HN, RS, MN, TB, TN, SL worked as a group to design the study, develop the plan for data abstraction and management; and/or plans for data analysis. DN, HD and HT were involved in data abstraction training, monitoring of data quality, and data cleaning and management. All coauthors were involved in data analysis and/or interpretation. TH and RS drafted the manuscript; HN, TB, and SL assisted with revising the manuscript. All authors critically reviewed the manuscript and approved the final version.

methamphetamine using versus non-using (AOR=2.68; 95%CI=1.08–6.65), were associated with increased odds of concurrent heroin use among patients.

Conclusion—The association between concurrent heroin use among MMT patients with the lack of family emotional/financial support recommends garnering family support is critical. Association with shorter heroin use history suggests motivational enhancement may reduce concurrent heroin use. Living with HIV, whether or not on ART, associated with increased concurrent heroin use suggests safe injection commodities and education, and drug-drug interaction management, are needed for this subgroup. Though few MMT clients reported baseline methamphetamine use, its association with later heroin use suggests the need for effective methamphetamine use interventions.

Keywords

Heroin use; Methadone maintenance treatment; Concurrent heroin use; HIV; ART

Background

People who inject drugs (PWID) account for the largest number of people living with HIV (PLHIV) and new HIV cases in Vietnam. The Vietnam Administration of HIV/AIDS Control (VAAC) reported that PWID accounted for about 36.1% of all newly identified HIV cases in 2015. Methadone maintenance treatment (MMT) is a highly effective intervention for reducing both heroin use and HIV transmission among PWID (Chen et al., 2013a; Farrell et al., 2005; Lawrinson et al., 2008; Wang, 2014; & Zou et al., 2015). In 2008, Vietnam established an MMT program to reduce heroin use and HIV transmission among PWID. By September 2016, 265 clinics operating in 62 provinces were serving approximately 50,000 patients. However, in 2014, the Vietnam Ministry of Public Security estimated that there were 140,000 heroin users across the country, thus, the need for MMT in the country remains high.

In Vietnam, criteria for admission into the MMT program [18] include: (1) medical diagnosis of opioid dependence; (2) no contraindications for methadone use; (3) age 18 years at admission; (4) written voluntary consent for participation in the program; and (5) not being prosecuted for or charged with a criminal offence during admission (the period between registration and induction).

According to the Ministry of Health (MOH) guidelines, all patients must present daily to MMT clinics to receive their methadone dose. In Vietnam, a patient is considered to have stopped methadone treatment if he/she missed at least 30 dose-days continuously; if a patient chooses to resume treatment after that point, he/she would be considered as a new patient. Clinicians are required to monitor concurrent heroin use among MMT patients at least monthly during the first 12 months and at least quarterly from then on (Vietnam Ministry of Health, 2010).

Concurrent heroin use among patients enrolled in MMT programs has been widely studied in many settings. Elsewhere, the proportion of those in opioid substitution programs found to be concurrently using opiates at 12 months is 22.5% in China (Chen et al., 2013a) and

29% in the United States (White et al., 2014). Previous studies in Vietnam identified a lower prevalence of concurrent heroin use among MMT patients in comparison with that in China and the United States (Chen et al., 2013a; Tran B et al., 2012; Tran H et al., 2015; & White et al., 2014). Factors associated with concurrent heroin use among MMT patients included history of opiate use prior to treatment (Darke et al., 2005; Tran B et al., 2012; & Wang et al., 2015), clinical factors (Baumeister et al., 2014; Lin et al., 2011; Lions et al., 2014; Lou et al., 2016; Tran B et al., 2012; & Tran H et al 2015) and family support at baseline (Lin et al., 2011; Luo et al., 2016; & Sullivan et al., 2014)..

Although the MMT program in Vietnam has been implemented since 2008, there are no national data on outcomes. Previous studies in Vietnam of outcomes of MMT—including the reduction of heroin use, program retention, and improvement of quality of life—were limited to one or two provinces. In addition, the rapid scale-up of the MMT program in Vietnam led to concerns that service quality might contribute to suboptimal treatment outcomes, including the increase of concurrent heroin use. Therefore, national data are needed to assess national level outcomes and inform more specific and targeted national strategies for reduction of continued heroin use. In this study, we sought to identify and understand factors associated with continued (i.e., concurrent) heroin use among MMT patients in Vietnam.

Methods

MMT monitoring procedure

Clinicians can assess concurrent heroin use by urine test or patient self-report. Urine tests will detect heroin use only when occurring within the two days since the last heroin dose (Smilh et al., 2000), whereas patients are asked to report on heroin use over the past month. Consequently, lab test results might not be consistent with self-report. Therefore, if a patient reports recent heroin use, urine testing is not always conducted. Information on concurrent heroin use should be documented in the patient charts for clinical decision-making; for example, to note the potential need to increase methadone dose. HIV status must be documented at baseline either with an official certificate of HIV positive status or by testing at the MMT clinic. For patients who refuse testing at baseline, they must be offered testing at each monthly/quarterly review session. During treatment, HIV-negative patients are to be retested for HIV every 6 months. Patients who are HIV-infected but not registered for HIV care are referred to the public HIV clinics.

Study design

We performed a retrospective cohort study of a nationally representative sample of patients enrolled in MMT during May 2008 through December 2013. Our goal was to assess concurrent heroin use among MMT patients in their first 24 months in treatment. Data were abstracted from patient charts by trained data abstractors using a standardized data collection tool. This study was formally reviewed at the U.S. Centers for Disease Control and Prevention and determined to be a program evaluation activity that did not require review by the Institutional Review Board.

Subject and sampling

Because we wanted to assess 24-month concurrent heroin use, only MMT clinics that started providing MMT before January 2012 — 24 months before the time of chart abstraction — were eligible for inclusion in this study. A total of 41 MMT clinics met this selection criterion. Within these eligible clinics, only patients who initiated MMT prior to January 2012 were eligible for inclusion. The total eligible patient population was 6,931.

Ten MMT clinics were selected from the 41 eligible clinics using the probability proportional to size (PPS) sampling method. In the second stage, 50 patients were selected by systematic random sampling from each selected clinic using the list of eligible patients.

Data collection and management and variable definition

Trained staff abstracted data from the charts of the 500 selected clients onto standardized abstraction forms. Abstraction forms were tailored to specific time periods for baseline (prior to treatment initiation) and periods of follow-up established for study data abstraction and analysis (see below). Information abstracted at baseline included demographics (age, sex, education level, employment status, marital status), family emotional/financial support (yes, no), total number of years and frequency of heroin use, methamphetamine use prior to MMT initiation, and HIV status (negative, positive but not on ART, and positive and on ART). Information on family emotional/financial support was assessed and documented by MMT counselors according to patients' self-report upon registration for treatment following the national standard counseling procedure.

Follow-up data abstracted included methadone dose, concurrent heroin use, methamphetamine use, HIV status (from official report or clinic testing), and ART status. Follow-up time periods for the purposes of abstraction and analysis were 0–3 months, 3–6 months, 6–12 months, and 12–24 months. The methadone dose for the last day of each time period was abstracted. Concurrent use of heroin was abstracted for the 30 days prior to the end of each time period (e.g., 60–90 days for the 0–3 month period). Missed methadone dose-days and HIV and ART status were abstracted anytime they were noted in charts during each of the follow-up periods. Data were double-entered using Epi-Info software, and all discrepancies were resolved. Illogical data were double checked with clinic staff and replaced with corrected data values.

A patient was considered to be using heroin concurrently with methadone if, during month 3, 6, 12, or 24 of treatment, he/she: 1) self-reported any heroin use; and/or 2) had any urine test positive for heroin as documented in the medical chart. To make results of our study consistent with WHO/UNODC/UNAIDS Technical Guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users (2012) and previous research (Baumeister et al., 2014), we categorized dosage as low (<60 mg/day), medium (60–100 mg/day), or high (>100 mg/day). Missed dose-days were dichotomized into “missed any dose-day” or “did not miss any dose-day” during each of these reviewed periods.

Data analysis

Data were analyzed using Stata [StataCorp. 2013. *Stata Statistical Software: Release 13.1*. College Station, TX: StataCorp LP]. All analyses controlled for the complex design of the survey. Survey (svy) procedures were used to estimate weighted proportions and 95% confidence intervals (CIs). While analyses accounted for clustering and a finite population correction (FPC) factor, the PPS design resulted in an equal probability of selection method (EPSEM) design (i.e., self-weighted), thereby obviating the need for sampling weights (Lehtonen et al., 2004).

Missing values were imputed using multiple imputation by chained equations (Van Buuren, 2007). The *mi impute chained* command was used to construct ten imputed datasets. The imputation model included age, marital status, educational level, employment status, family support, number of years of heroin use prior to MMT initiation, frequency of heroin use 30 days prior to admission, methadone dose, concurrent heroin use, missed dose-day during treatment and HIV status as defined above. All data were assumed missing at random (MAR) (Schafer and Graham, 2002). Estimates were combined using Rubin's rule (Rubin, 1987).

A three-level, random-effects logistic regression model was used to assess risk factors for concurrent heroin use after methadone treatment initiation. Random-effects were specified on the intercept for patients and facilities. Time was modeled as a categorical variable and included in all analyses; logistic regression models were unweighted and did not account for FPC. Factors reported in the literature to be associated with heroin use during methadone treatment were screened for inclusion in the multivariable model. These included age, education level, employment status, marital status at admission, family support at admission, total number of years and frequency of heroin use prior to treatment initiation, methadone dose, missed methadone dose-days, and HIV status. Variables with p-value < 0.25 were included in the initial multivariable model, which were some demographic characteristics, heroin use history and clinical factors except missed any dose-day as it is very much correlated to heroin use in actual. Variables with the largest p-value were excluded from the multivariable model one at a time and the model was refit until all factors were associated with concurrent heroin use at p<0.05. Interactions between time and each of variable in the multivariable model were examined.

Results

Baseline demographic, drug use characteristics and HIV status

Of patients enrolled in MMT from May 2008 to December 2013, 96.8% were male and 79.8% were aged <40 years when they initiated MMT (Table 1). About 44% of all patients had completed 10th grade or higher education. Over half of the patients were married or living with a partner as a couple (52%), and 54.2% were employed either full-time or part-time. Most patients received financial and/or emotional support from their family members (92.4%). Prior to treatment initiation, 33.3% of patients were identified as HIV infected, approximately half of whom (48.0%) were on ART. Information on education, marriage,

employment, family support, methamphetamine use and HIV status was missing among a part of patients but all these data were imputed as in Table 1.

In general, patients reported long periods of opiate use prior to treatment initiation. One half of patients had used heroin for over 10 years before MMT initiation, 16.4% of all patients had used heroin for 15 years or longer before treatment. Within the 30 days prior to treatment admission, all patients used heroin daily; 31.2% used four or more times a day. A minority of patients reported any methamphetamine use at treatment initiation (2.9%).

Concurrent heroin use and other clinical outcomes over 24 months

Of 500 heroin users at baseline, 59 were lost to follow-up during the 24 months: 3 cases during months 0–3; 5 cases during months 4–6; 19 cases during months 7–12; and 32 cases during months 13–24. Reasons for lost to follow-up included: 1) being put in jail or mandatory detoxification (19 cases); 2) voluntary cessation of treatment (9 cases); 3) moved to other clinics (8 cases); 4) died (5 cases); or 5) had no documented reason (18 cases).

The estimated percentage of patients who used heroin concurrently with methadone treatment was 54.9% during the third month, 18.9% during the sixth month, 14.5% during the twelfth month, and 15.4% during the 24th month. Only one or two patients reported methamphetamine use during the first 24 months on MMT (Table 2).

Approximately one-third of MMT clients were known to be HIV-infected and this proportion remained consistent across the time periods. Nearly a fifth of patients (17.4%) did not accept HIV testing at admission; therefore, clinicians continuously offered HIV testing and identified four additional HIV-positive patients over the 24-month follow-up period. By the end of month 24, 71 patients (14.8%, unweighted) still had not been HIV tested (or did not have test results recorded in their charts). Of all patients remained in treatment, we observed an increase in the percentage of HIV-infected patients on ART from 12.8% at baseline to 18.2% at month 24. However, after 24 months of MMT, 15.1% of all patients remained treatment were HIV-positive but not yet on ART¹.

The percentage of patients with methadone doses of 60 mg a day was 70.0% at the end of month 3, 73.2% at the end of month 6, and 69.9% at the end of month 12, but was only 60.9% at the end of month 24. The percentage of patients who missed at least one dose-day was: 5.0% during months 0–3, 16.4% during months 4–6, 25.2% during months 7–12, and 35.0% during months 13–24. Of all patients, the percentage of those who missed 1–3 doses consecutively was 3.8% during months 0–3, 14.8% during months 4–6, 22.4% during months 7–12, and 31.6% during month 13–24. The percentage of patient who missed 4–5 doses consecutively was: 0.8% during months 0–3, 1.2% during months 3–6, 1.8% during months 7–12, and 2.2% during months 13–24. Percentage of missing 6 doses or more consecutively during these time periods were 0.4%, 0.8%, 2.6% and 3.6%, respectively.

¹Some HIV-infected patients might not have been eligible for ART. National HIV treatment guidelines at the time of this study included CD4 <350 cells/mm³ or WHO stage III or IV disease. MMT charts do not contain this information; therefore, we are unable to assess how many of the HIV-positive patients were eligible for ART.

Information on concurrent heroin use, methamphetamine use, HIV status, methadone dose and missing dose-day was not available among a proportion of patients at different follow-up periods and all missing information was imputed as in Table 2.

Factors associated with concurrent heroin use over 24 months

Unadjusted analysis showed that no family support at baseline, being HIV positive (regardless of ART enrollment), methamphetamine use before treatment initiation, missing any dose-days during the 24 months in treatment, and having a methadone dose of over 100mg/day increased the odds of heroin use over the first 24 months on MMT (Table 3). In multivariable analysis, having no family support at baseline (AOR = 2.03; 95% CI: 1.17–3.53), using heroin for less than 15 years (AOR = 1.55; 95% CI: 1.01–2.38), methamphetamine use before treatment initiation (AOR = 2.68; 95% CI: 1.08–6.65), living with HIV/on ART (AOR = 2.39, 95% CI: 1.61–3.55), and living with HIV/not on ART (AOR = 1.79, 95% CI: 1.07–2.98) were all associated with increased the odds of heroin use over the first 24 months on MMT. No significant interactions were observed between variables in the final multivariable model and time.

Discussion

The study describes the first investigation of factors associated with concurrent heroin use among a nationally representative sample of Vietnam's national MMT program. Abstraction of data from existing medical records was found to be feasible and convenient to implement. In this first nationally representative sample of MMT patients in Vietnam, we observed a sharp reduction of heroin use among patients on MMT after treatment initiation, which was maintained at a very low level as they continued treatment. Lower concurrent heroin use among MMT patients in Vietnam may be a result of higher average methadone dose: 91.6 mg/day at month 12 compared with 52.4 mg/day in China (Chen et al., 2013a); and 86.4 mg/day at month 24 compared with 60–70 mg/day in Switzerland (Dobler-Mikola et al. 2005). In addition, in Vietnam, relapse prevention counseling is provided by MMT counselors on a regular basis, which may also contribute to lower observed concurrent heroin use.

Very few patients self-reported using methamphetamine prior to MMT initiation and only one or two patients self-reported methamphetamine use during treatment. However, the use of methamphetamine may be underestimated as no urine test was used to monitor methamphetamine use among MMT patients during the timeframe of this study. Also of concern is the increased use of methamphetamine in Vietnam in recent years (The Ministry of Public Security of Vietnam)

In this study, being HIV infected whether on ART or not, used methamphetamine at baseline, lack of family support at baseline, and shorter duration of heroin use prior to MMT initiation were all associated with increased odds of concurrent heroin use among MMT patients. Missing any dose-day was associated with concurrent heroin use (Luo et al., 2016; & Tran H et al., 2015) but this factor is strongly correlated with concurrent heroin use so we did not include this factor in our multivariable model.

Methamphetamine use along with heroin before treatment initiation, even with a small proportion, associated with increase odds of concurrent heroin may be an important predictor. It suggests that MMT providers may need special care about methamphetamine use when patients register for treatment and urine test for methamphetamine use may be needed. This finding has not been reported by any previous study in the region. One study in China reported 12.9% of MMT patients used methamphetamine during treatment (Wang R et al. 2015), however, the study did not evaluate the association between methamphetamine use and concurrent heroin use. While the use of methamphetamine in Vietnam is increasing, this finding provides important evidence that to maintain low proportion of concurrent heroin use, MMT providers may need to address methamphetamine and other substances use disorders among MMT patients. MMT providers in Vietnam may need to provide clients with evidence-based treatment therapies for methamphetamine use including contingency management (Roll J. M. 2007), intensive motivational interviewing, cognitive behavioral therapy, or combine therapies (Hill R. 2015).

The higher frequency of concurrent heroin use among those living with HIV but not yet on ART, however, has not yet been explained by any previous study. Further psycho-biological or qualitative research may be warranted to elucidate this association. In our study, we could not compare heroin use among HIV-infected PWID who were on MMT with those who were not. However, a Canadian study among HIV-positive PWID revealed that being on MMT was associated with reduced heroin injection frequency, borrowing syringes and non-fatal overdose (Pettes et al., 2010). Nonetheless, concurrent heroin use among HIV-infected PWID carries a risk of transmitting HIV to other PWID if contaminated injection devices are shared. Therefore, specific safe injection strategies and a supply of clean needles and syringes are needed for this group of patients to prevent HIV transmission. In this era of “Test and Treat” to meet UNAIDS 90-90-90 targets, all HIV-positive MMT patients should be initiated on ART as soon as possible to reduce morbidity as well as the risk of HIV transmission to others (Fraser et al., 2016).

Similar to other studies in Vietnam (Tran B et al., 2012; & Tran VH et al., 2015), we found that HIV-infected patients on ART were more likely than HIV-negative patients to be using heroin concurrently with methadone. That some ARVs (e.g., efavirenz and nevirapine) induce methadone metabolism is well documented (Clarke et al., 2001; Gruber and McCance-Katz, 2010; McCance-Katz et al., 2010; & Stocker et al., 2004) therefore, patients who are on ART may have a lower blood concentration of methadone, which might explain their need to use heroin concurrently to reduce symptoms of withdrawal or cravings.

Our study revealed that a lack of emotional and/or financial support from family members at baseline was also associated with concurrent heroin use among MMT patients. This finding is consistent with findings from other studies (Baumeister et al. 2014; Lin et al., 2011; & Luo et al., 2016). Additional studies conducted in two provinces of Vietnam also reported that MMT patients with unstable family status were more likely to continue using heroin (Tran B et al., 2012; & Tran VH et al., 2015). These findings suggest that strategies to establish family support to patients before or soon after treatment initiation might help MMT patients to reduce later concurrent heroin use. If the establishment of family support to patients is not possible, treatment providers may consider offering additional psychosocial

support, such as contingency management (Chen et al., 2013b) or peer support groups (Tracy and Wallace, 2016).

One other factor that we found associated with increased concurrent heroin use was a shorter history of heroin use before MMT initiation. This finding is similar to one study in Yunnan, China (Wang et al. 2015), which showed a lower prevalence of concurrent heroin use among patients who had longer length of heroin use before MMT. Enhanced treatment literacy and psychoeducation, contingency management, and motivation enhancement (Chen et al., 2013b; & Zhang et al., 2016) may be helpful to help patients with shorter history of heroin use.

Limitations

Our study has several limitations. In this analysis of secondary data, information abstracted from MMT clinical records was dependent on the completeness and quality of clinical information documented by the clinicians. We did not interview patients or clinicians to validate abstracted information. Thus, it is possible that we were not able to accurately capture other important information. Although a proportion of data was missing, after imputation, our study results are similar to those of previous studies in Vietnam. Concurrent heroin use among MMT patients, the main study outcome, was available for 75–87.9% of all observations at different reviewing periods. This missing data may have caused overestimation of concurrent heroin use as physicians and counselors are more likely to forget documenting heroin use status in the chart when the patient did not use. Furthermore, 59 patients were lost to follow-up at two years (11.8%). Loss to follow up may bias the possible associations between concurrent heroin use and our measured covariates. Similarly, we do not know whether HIV-infected MMT patients who were not on ART were eligible for ART. We did not have adequate data on other substance use and psychiatric comorbidities in our database and thus could not perform analysis to find a possible association between these factors and concurrent heroin use.

That a proportion of records were incomplete reflects that the quality of documentation of clinical practice did not meet with the minimum standard set by the Ministry of Health of Vietnam. We also noted that a number of MMT patients were not tested for HIV; this is inconsistent with national guidelines. Our investigation therefore has helped to highlight the need for more intensive national quality assurance strategies, especially as the MMT program continues its rapid expansion in Vietnam.

Conclusions

We found that methamphetamine use along with heroin, even prior to MMT initiation is associated with concurrent heroin use among MMT patients in Vietnam. In addition, concurrent heroin use is also associated with being HIV infected, whether on ART or not, a lack of emotional and/or financial support from their family members at baseline, and shorter history of heroin use before treatment. In order to reduce concurrent heroin use among MMT patients, we recommend MMT providers to provide effective treatment therapies for methamphetamine use, strengthen efforts to improve family support to patients

during treatment or else find effective alternatives to family support, improve adherence to treatment, improve the coverage of ART among patients and promote better management of drug-drug interaction between ARVs and methadone. Patients with a shorter history of heroin use will need strengthened motivational enhancement to reduce concurrent use. In the meantime, specific harm reduction strategies for patients living with HIV are needed to prevent onward HIV transmission to other PWID through safe injection education, supply of clean needles and syringes, and promotion of low dead space syringes (Vickerman et al., 2013; & Zule et al., 2012).

As a result of this investigation, we have confirmed the value of examining routinely collected data for measuring important public health outcomes and processes. By routinely assessing programmatic data, clinicians may detect gaps in clinical practice and build upon opportunities to improve quality of services.

Acknowledgments

The authors thank the Vietnam Administration for HIV/AIDS Control for coordinating data abstraction and management. We also thank the MMT clinic staff from the selected clinics who documented daily data in patients' records and supplied to the study.

This study project has been supported by the President's Emergency Plan for AIDS Relief (PEPFAR) through U.S. Centers for Disease Control and Prevention (CDC) under the terms of the Cooperative Agreement #9976/U2GH001016-02. This study was formally reviewed at the U.S. Centers for Disease Control and Prevention and determined to be a program evaluation activity that did not require review by the Institutional Review Board.

The dataset used and/or analyzed during this study is available from corresponding author on reasonable request.

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
ART	Antiretroviral Treatment
ARV	Antiretroviral Drugs
CDC	The U.S Centers for Diseases Control and Prevention
CI	Confidence Intervals
FPC	Finite Population Correction
HIV	Human Immunodeficiency Virus
MAR	Missing at Random
MMT	Methadone Maintenance Treatment
OR	Odds Ratio
PEPFAR	The President's Emergency Plan for AIDS Relief
PLHIV	People Living with HIV

PWID	People Who Inject Drug
PPS	Probability Proportional to Size
UNODC	The United Nations Office on Drug and Crime
UNAIDS	The Joint United Nations Programme on HIV/AIDS
VAAC	The Vietnam Administration of HIV/AIDS Control
WHO	The World Health Organization

References

1. Baumeister M, Vogel M, Dürsteler-MacFarland KM, Gerhard U, Strasser J, Walter M, et al. Association between methadone dose and concomitant cocaine use in methadone maintenance treatment: A register-based study. *Substance Abuse Treatment, Prevention, and Policy*. 2014; 9:46.
2. Chen W, Hong Y, Zou X, McLaughlin MM, Xia Y, Ling L. Effectiveness of prize-based contingency management in a methadone maintenance program in China. *Drug and Alcohol Dependence*. 2013; 133:270–274. [PubMed: 23831409]
3. Chen W, Xia Y, Hong Y, Hall B, Ling L. Predictors of continued HIV-risk behaviors among drug users in methadone maintenance therapy program in China—A prospective study. *Harm Reduction Journal*. 2013; 10:23. [PubMed: 24107380]
4. Clarke M, Mulcahy M, Tjia J, Reynolds E, Gibbons E, Barry G, et al. The pharmacokinetics of methadone in HIV-positive patients receiving the non-nucleoside reverse transcriptase inhibitor efavirenz. *British Journal of Clinical Pharmacology*. 2001; 51:213–217. [PubMed: 11298066]
5. Darke S, Ross J, Teesson M, Ali R, Cooke R, Ritter A, et al. Factors associated with 12 months continuous heroin abstinence: Findings from the Australian Treatment Outcome Study (ATOS). *The Journal of Substance Abuse Treatment*. 2005; 28:255–263. [PubMed: 15857726]
6. Dobler-Mikola A, Hattenschwiler J, Meili D, Beck T, Boni E, Modestin J. Patterns of heroin, cocaine, and alcohol abuse during long-term methadone maintenance treatment. *Journal of Substance Abuse Treatment*. 2005; 29:259–265. [PubMed: 16311178]
7. Farrell M, Gowing L, Marsden J, Ling W, Ali R. Effectiveness of drug dependence treatment in HIV prevention. *International Journal of Drug Policy*. 2005; 16:S67–S75.
8. Fraser, H., Mukandavire, C., Martin, N., Hickman, M., Cohen, M., Miller, W., et al. HIV treatment as prevention among people who inject drugs – A re-evaluation of the evidence; *International Journal of Epidemiology*. 2016. p. 1-13. <https://doi.org/10.1093/ije/dyw180>
9. Gruber A, McCance-Katz F. Methadone, buprenorphine, and street drug interactions with antiretroviral medications. *Current HIV/AIDS Report*. 2010; 7:152–160.
10. Hill, R. Evidence-based practices for treatment of methamphetamine dependency: A review. Community Engaged Scholarship Institute; Guelph, ON: 2015. <https://atrium.lib.uoguelph.ca/xmlui/handle/10214/8902>
11. Lawrinson P, Ali R, Buavirat A, Chiamwongpaet S, Dvoryak S, Habrat B, et al. Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. *Addiction*. 2008; 103:1484–1492. [PubMed: 18636999]
12. Lehtonen, R., Pahkinen, E. Practical methods for design and analysis of complex surveys. John Wiley & Sons, Ltd.; Chichester, England: 2004. p. 172-173.
13. Lin C, Wu Z, Detels R. Family support, quality of life and concurrent substance use among methadone maintenance therapy clients in China. *Public Health*. 2011; 125(5):269–274. [PubMed: 21414646]
14. Lions C, Carrieri MP, Michel L, Mora M, Marcellin F, Morel A, et al. Predictors of non-prescribed opioid use after one year of methadone treatment: An attributable-risk approach (ANRS-Methaville trial). *Drug and Alcohol Dependence*. Feb.2014 135:1–8. [PubMed: 24268548]

15. Luo X, Zhao P, Gong X, Zhang L, Tang W, Zou X, et al. Concurrent heroin use and correlates among methadone maintenance treatment clients: A 12-month follow-up study in Guangdong Province, China. *International Journal of Environmental Research and Public Health*. 2016; 13:305. <https://doi.org/10.3390/ijerph13030305>.
16. McCance-Katz F, Sullivan L, Nallani S. Drug interactions of clinical importance among the opioids, methadone and buprenorphine, and other frequently prescribed medications: A Review. *American Journal on Addictions*. 2010; 19(1):4–16. [PubMed: 20132117]
17. Pettes T, Wood E, Guillemi S, Lai C, Math M, Montaner J, et al. Methadone use among HIV-positive injection drug users in a Canadian setting. *Journal of Substance Abuse Treatment*. 2010; 39(2):174–179. <https://doi.org/10.1016/j.jsat.2010.05.001>. [PubMed: 20598827]
18. Roll JM. Contingency management: An evidence-based component of methamphetamine use disorder treatments. *Addiction*. 2007; 102:114–120. <https://doi.org/10.1111/j.1360-0443.2006.01774.x>.
19. Rubin, B. Multiple imputation for nonresponse in surveys. Vol. xxix. Wiley; New York: 1987. 1987. p. 258
20. Schafer JL, Graham JW. Missing data: Our view of the state of the art. *Psychological Methods*. 2002; 7(2):147–177. [PubMed: 12090408]
21. Smilh ML, Shimomura ET, Summers J, Paul BD. Detection times and analytical performance of commercial urine opiate immunoassays following heroin administration. *Journal of Analytical Toxicology*. 2000; 24:522–529. [PubMed: 11043654]
22. Stocker H, Kruse G, Kreckel P, Herzmann C, Arasteh K, Claus J, et al. Nevirapine significantly reduces the levels of racemic methadone and (R)-methadone in human immunodeficiency virus-infected patients. *Antimicrobial Agents and Chemotherapy*. 2004:4148–4153. [PubMed: 15504834]
23. Sullivan S, Wu Z, Cao X, Liu E, Detels R. Continued drug use during methadone treatment in China: A retrospective analysis of 19,026 service users. *Journal of Substance Abuse Treatment*. 2014; 47(1):86–92. <https://doi.org/10.1016/j.jsat.2013.12.004>. [PubMed: 24629884]
24. Tracy K, Wallace SP. Benefits of peer support groups in the treatment of addiction. *Substance Abuse and Rehabilitation*. 2016; 7:143–154. [PubMed: 27729825]
25. Tran B, Ohinmaa A, Mills S, Duong A, Nguyen L. Multilevel predictors of concurrent opioid use during methadone maintenance treatment among drug users with HIV/AIDS. *PLoS ONE*. 7(12):e51569.
26. Tran H, Tran T, Tran M, Nguyen N, Nguyen Q, Nguyen M, et al. Impact of a methadone maintenance therapy pilot in Vietnam and its role in a scaled-up response. *Harm Reduction Journal*. 2015; 12:39. [PubMed: 26471235]
27. Van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. *Statistical Methods in Medical Research*. 2007; 16(3):219–242. <https://doi.org/10.1177/0962280206074463>, pmid:17621469. [PubMed: 17621469]
28. Vickerman P, Martin NK, Hickman M. Could low dead-space syringes really reduce HIV transmission to low levels? *International Journal of Drug Policy*. 2013; 24:8–14. [PubMed: 23206493]
29. Wang L, Wei X, Wang X, Li J, Li H, et al. Long-term effects of methadone maintenance treatment with different psychosocial intervention models. *PLoS ONE*. 2014; 9(2):e87931. <https://doi.org/10.1371/journal.pone.0087931>. [PubMed: 24498406]
30. Wang R, Ding Y, Bai H, Duan S, Ye R, Yang Y, et al. Illicit heroin and methamphetamine use among methadone maintenance treatment patients in Dehong prefecture of Yunnan Province, China. *PLoS ONE*. 2015; 10(7):e0133431. <https://doi.org/10.1371/journal.pone.0133431>. [PubMed: 26196394]
31. White W, Campbell M, Spencerc R, Hoffman H, Crissman B, DuPont R. Patterns of abstinence or continued drug use among methadone maintenance patients and their relation to treatment retention. *Journal of Psychoactive Drugs*. 2014; 46(2):114–122. [PubMed: 25052787]
32. Zhang B, Cai T, Yan Z, Mburu G, Wang B, Yang L. Impact of blended treatment literacy and psychoeducation on methadone maintenance outcomes in Yunnan, China. *Harm Reduction Journal*. 2016; 13:8. <https://doi.org/10.1186/s12954-016-0097-y>. [PubMed: 26915361]

33. Zou X, Ling L, Zhang L. Trends and risk factors for HIV, HCV and syphilis seroconversion among drug users in a methadone maintenance treatment programme in China: A 7-year retrospective cohort study. *BMJ Open*. 2015; 5:e008162. <https://doi.org/10.1136/bmjopen-2015-008162>.
34. Zule, WA., Cross, HE., Stover, J., Pretorius, C. Are major reductions in new HIV infections possible with people who inject drugs? The case for low dead-space syringes in highly affected countries. *International Journal of Drug Policy*. 2012. <http://dx.doi.org/10.1016/j.drugpo.2012.07.002>

Table 1

Baseline demographic, heroin use characteristics, HIV status among nationally representative sample of MMT patients in Vietnam, 2008–2013.

Variables	N	n	Weighted Proportion (95% CI)	Multiple Imputation (N=500) Proportion (95% CI)
Gender				
Male	500	484	96.8 (92.1 – 98.7)	96.8 (93.8 – 99.8)
Female	500	16	3.2 (1.3 – 7.9)	3.2 (0.2 – 6.2)
Missing	500	0	0	--
Age (years)				
Under 40	500	399	79.8 (72.6 – 85.5)	79.8 (73.2 – 86.4)
40 or older	500	101	20.2 (14.5 – 27.4)	20.2 (13.6 – 26.8)
Missing	500	0	0	--
Education				
Junior high school (grade 6 – 9) or lower	470	264	56.2 (45.0 – 66.8)	56.1 (44.6 – 67.5)
High school (grade 10 – 12) or higher	470	206	43.8 (33.2 – 55.0)	43.9 (32.5 – 55.4)
Missing	500	30	6.0 *	--
Marriage				
Married or living with partner as couple	479	249	52.0 (41.3 – 62.5)	52.0 (40.8 – 63.3)
Single/Separated/ Divorced	479	230	48.0 (37.5 – 58.7)	48.0 (36.7 – 59.2)
Missing	500	21	4.2 *	--
Employment				
Yes (Full-time or Part-time)	473	255	53.9 (46.6 – 61.1)	54.2 (46.5 – 61.9)
Unemployed	473	218	46.1 (38.9 – 53.4)	45.8 (38.1 – 53.5)
Missing	500	27	5.4 *	--
Had financial and/or emotional support from family				
Yes	434	403	92.9 (86.9 – 96.2)	92.4 (87.7 – 97.3)
No	434	31	7.1 (3.8 – 13.1)	7.6 (2.7 – 12.4)
Missing	500	66	13.2 *	--
Number of years used heroin prior to MMT initiation				
Less than 5 years	500	80	16.0 (9.7 – 25.3)	16.0 (8.0 – 24.0)
5 years to less than 10 years	500	167	33.4 (28.0 – 39.3)	33.4 (27.5 – 39.3)
10 years to less than 15 years	500	171	34.2 (26.7 – 42.5)	34.2 (26.0 – 42.4)
15 years or longer	500	82	16.4 (12.1 – 21.8)	16.4 (11.4 – 21.4)
Missing	500	0	0	--
Frequency of heroin use 30 days prior to admission				
1–3 times a day	500	344	68.8 (63.6 – 73.6)	68.8 (63.7 – 73.9)
4 times or more a day	500	156	31.2 (26.4 – 36.4)	31.2 (26.1 – 36.3)
Missing	500	0	0	--
Methamphetamine use				
Yes	467	12	2.6 (1.2 – 5.5)	2.9 (0.4 – 5.4)
No	467	455	97.4 (94.5 – 98.8)	97.1 (94.6 – 99.6)

Variables	N	n	Weighted Proportion (95% CI)	Multiple Imputation (N=500) Proportion (95% CI)
Missing	500	33	6.6 [*]	--
HIV status				
Negative	412	274	66.5 (56.8 – 75.0)	66.7 (57.1 – 76.2)
Positive	412	138	33.5 (25.0 – 43.2)	33.3 (26.2 – 44.1)
Positive, not on ART	412	73	17.7 (11.0 – 27.4)	17.3 (9.8 – 24.7)
Positive, on ART	412	65	15.8 (10.1 – 23.8)	16.0 (7.4 – 24.8)
Missing	500	88	17.6 [‡]	--

^{*} Missing due to no information documented in patient chart

[‡] Missing because patients refused HIV testing

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Concurrent heroin use, clinical outcomes over 24 months among nationally representative sample of MMT patients in Vietnam, 2008–2013

Clinical Outcomes	3-month			6-month			12-month			24-month		
	N	n	Weighted Proportion (95%CI)	N	n	Weighted Proportion (95%CI)	N	n	Weighted Proportion (95%CI)	N	n	Weighted Proportion (95%CI)
HIV status												
Negative	420	279	67.1 (57.6–75.0)		282	67.1 (58.2–75.0)		280	67.2 (57.8–75.3)		268	66.7 (57.8–74.5)
Positive	420	138	32.9 (25.0–41.8)	420	138	32.9 (25.0–41.8)	417	137	32.8 (24.7–42.2)	402	134	33.3 (25.5–42.2)
Positive, not on ART	420	67	16.0 (9.7–25.0)	420	62	14.8 (8.8–23.8)	417	58	13.9 (8.1–22.8)	402	53	13.2 (7.3–22.7)
Positive, on ART	420	71	16.9 (11.1–24.9)	420	76	18.1 (11.9–26.5)	417	79	18.9 (12.9–26.9)	402	81	20.1 (14.2–27.9)
Missing *	500	80	16.0	--	497	15.5	--	492	15.2	--	473	14.8
Methadone dose												
<60mg a day	498	149	29.9 (21.4–40.1)		131	26.7 (20.0–34.7)		143	29.7 (22.8–37.6)		179	39.1 (30.9–47.9)
60 – 100mg a day	498	221	44.4 (39.8–49.0)	491	223	45.4 (41.3–49.6)	482	197	40.9 (35.2–46.8)	458	159	34.7 (27.5–42.7)
>100mg a day	498	128	25.7 (16.7–37.4)	491	137	27.9 (20.5–36.8)	482	142	29.4 (21.7–38.6)	458	120	26.2 (19.2–34.7)
Missing *	500	2	0.4	--	497	1.2	--	492	2.0	--	473	3.2
Missed dose-days												
Yes	500	25	5.0 (2.7–9.0)		81	16.4 (10.4–24.9)		118	27.0 (17.5–39.2)		144	35.0 (25.8–45.5)
1–3 doses consecutively	500	19	3.8 (2.1–6.9)	493	73	14.8 (9.1–23.1)	437	104	23.8 (15.7–34.9)	411	127	30.9 (21.8–41.8)
4–5 doses consecutively	500	4	0.8 (0.4–1.8)	493	6	1.2 (0.4–3.6)	437	9	2.1 (0.6–7.2)	411	11	2.7 (1.2–5.9)
6 doses consecutively	500	2	0.4 (0.1–1.5)	493	4	0.8 (0.2–3.6)	437	13	3.0 (1.6–5.6)	411	18	4.4 (2.5–7.5)
No	500	475	95.0 (91.0–97.3)	493	412	83.6 (75.1–89.6)	437	319	73.0 (60.8–82.5)	411	267	65.0 (54.5–74.2)
Missing *	500	0	0	--	497	0.8	--	492	11.2	--	473	13.1
Methamphetamine use												
Yes	489	0	0	--	483	0.2 (0 – 1.5)99.8	337	2	0.6 (0.2 – 2.2)	460	1	0.2 (0 – 0.6)
No	489	489	100	--	483	14 (98.5 – 100)2.8	337	335	99.4 (97.8 – 99.8)	460	459	99.8 (98.5 – 100)
Missing *	497	8	1.6	--	497		--	492	31.5	--	473	2.7
Concurrent Heroin use												
Yes	437	237	54.2 (42.4–65.6)		79	19.2 (12.4–28.4)		59	14.5 (8.5–23.5)		45	13.2 (9.4–18.1)
No	437	200	45.8 (34.4–57.6)	412	333	80.8 (71.6–87.6)	408	349	85.5 (76.5–91.5)	342	297	86.8 (81.9–90.6)
				412	333	45.3 (33.8 – 56.9)	408	342	85.4 (77.5 – 93.4)	342	297	84.8 (78.2 – 91.3)

Table 3

Factors associated with concurrent heroin use over 24 months among nationally representative sample of MMT patients in Vietnam, 2008–2013.

Related factors	Multiple Imputation (N=500)			
	Crude Odd Ratio (95%CI)	p-value	Adjusted Odd Ratio (95% CI)	p-value
<i>Time of assessment</i>				
Month 3	1		1	
Month 6	0.15 (0.10 – 0.22)	<0.001	0.14 (0.10 – 0.21)	<0.001
Month 12	0.10 (0.07 – 0.16)	<0.001	0.10 (0.07 – 0.15)	<0.001
Month 24	0.11 (0.08 – 0.17)	<0.001	0.11 (0.07 – 0.17)	<0.001
<i>Age at MMT initiation</i>				
Under 40	1.46 (0.98 – 2.18)	0.060		
40 or older	1			
<i>Baseline marriage</i>				
Married/living with partner as couple	1.00 (0.71 – 1.39)	0.981		
Single/Separated/ Divorced	1			
<i>Baseline educational level</i>				
Junior high school (grade 6–9) or lower	1			
High school (grade 10–12) or higher	0.85 (0.61 – 1.19)	0.341		
<i>Employment</i>				
Yes (Full-time or Part-time)	1.21 (0.88 – 1.67)	0.239		
Unemployed	1			
<i>Family support at baseline</i>				
Yes	1		1	
No	2.08 (1.18 – 3.67)	0.012	2.03 (1.17 – 3.53)	0.012
<i>Number of years used heroin prior to MMT initiation</i>				
Less than 15 years	1.55 (1.00 – 2.40)	0.054	1.55 (1.01 – 2.38)	0.044
15 years or longer	1		1	
<i>Frequency of heroin use 30 days prior to MMT initiation</i>				
1 – 3 times a day	1			
4 times or more a day	0.92 (0.66 – 1.27)	0.610		
<i>Missed any dose-day</i>				
Yes	1.50 (1.02 – 2.21)	0.042		
No	1			
<i>Methamphetamine use prior to MMT initiation</i>				
Yes	2.79 (1.11 – 7.00)	0.030	2.68 (1.08 – 6.65)	0.034
No	1		1	
<i>Methadone dose</i>				
< 60mg/day	1			
60 – 100mg/day	1.10 (0.76 – 1.59)	0.629		
>100mg/day	1.75 (1.12 – 2.72)	0.014		

Related factors	Multiple Imputation (N=500)			
	Crude Odd Ratio (95%CI)	<i>p</i> -value	Adjusted Odd Ratio (95% CI)	<i>p</i> -value
<i>HIV status</i>				
Negative	1		1	
Positive, not on ART	1.73 (1.03 – 2.89)	0.037	1.79 (1.07 – 2.98)	0.027
Positive, on ART	2.48 (1.61 – 3.83)	<0.001	2.39 (1.61 – 3.55)	<0.001